

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/003033

International filing date (day/month/year)
22.03.2005

Priority date (day/month/year)
22.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/192, C07C59/64

Applicant
KARO BIO AB

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

10/593928
IAP6 Rec'd PCT/PTO 21 SEP 2006

International application No.
PCT/EP2005/003033

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. -

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. -
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/003033

**Box No. V Reasoned statement under Rule 43b/s.1(a)(I) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-20
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-20
Industrial applicability (IA)	Yes: Claims	1-5,8-10,14-20
	No: Claims	

2. Citations and explanations

see separate sheet

Re Section III

Claims 6,7,11-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 6,7,12,13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

However, claim 11 is directed to a diagnostic method.

Re Section V

Novelty and inventive step

D1: WO 01/36365 A (APELQVIST THERESA ; GORDON SANDRA (SE); HEDFORS ASA (SE); BRANDT PETER) 25 May 2001 (2001-05-25)

The present application is directed to a compounds according to formula (I), (Ia) and (Ib) (cf. claims 1,3 and 4 respectively), first or second medical use of the compounds (cf. claims 5-8,13), a diagnostic method (cf. claim 11), an in vitro method (cf. claim 12), pharmaceutical compositions or formulations (cf. claims 9,10,16-20) as well as methods for the preparation of the compounds (cf. claims 14,15).

D1 (cf. passages cited in the SR) represents the closest prior art and discloses compounds of formulae (I), (Ia), (Ib) with $w = C_2$ alkylene, $R^5 = COOR^c$ with $R^c = H$, $R^3 = R^4 = Br$, $Y = O$, $Y' = CH_2$, $n = 0$, $R^1 = H, Et$. Moreover, the D1 discloses the use of the above mentioned compounds in the field of treatment or prophylaxis of conditions associated with a disease or disorder associated with thyroid receptor activity, as well as pharmaceutical formulations

and pharmaceutical formulations showing retoid or vitamin D additives. D1 (cf. passages cited in the ISR) discloses also the preparation of the compounds either by reduction of a nitro function to the corresponding amine, or as outlined in example 105.

However, in claim 1 the compounds with $w = C_2$ alkylene, $R^5 = COOR^c$ with $R^c = H$, $R^3 = R^4 = Br$, $Y = O$, $Y' = CH_2$, $n = 0$, $R^1 = H, Et$ have been disclaimed.

Consequently, the matter of claim 1 is novel. Since all the other claims refer to the compounds in claim 1, claims 2-20 are also novel.

Therefore the technical problem may be regarded as the provision of further compound showing thyroid receptor activity.

The solution given in claim 1 is not considered of involving an inventive step, because the compounds with $R^1 = -CH_3$ or $-CH_2-CH_2-CH_3$ are structurally so closely related to compounds with $R^1 = -CH_2-CH_3$ that it is obvious for the skilled person that the ethyl derivative ($R^1 = -CH_2-CH_3$) and the methyl ($R^1 = -CH_3$) and propyl ($R^1 = -CH_2-CH_2-CH_3$) derivatives will show the same properties.

Claims 2-13 do not add any features which can establish inventive activity over D1. The method for preparing the compounds is directly deducible for the skilled person in the art from D1 (cf. passages cited in the ISR) Claims 16-20 are also not inventive, because the addition of known therapeutic agent to a composition cannot be regarded of involving an inventive step.

Thus the subject matter of claims 1-20 does not fulfil the criteria of Article 33(3) PCT.